

REMARKS

This amendment is responsive to the final Office Action mailed January 8, 2004. Original Claims 1-11 are under examination in the present action. Claims 1-5, 7, 8, 10 and 11 stand rejected. Claims 6 and 9 are objected to for being dependent on a rejected base claim.

The Examiner also objects to the specification and requests that Applicants update the status of referenced U.S. patent applications. Applicants have herein amended the specification to update the status of the U.S. applications where appropriate. Withdrawal of the objection to the specification is believed to be in order.

Pursuant to the Examiner's point 5 on page 5 of the Office Action, Applicants have amended Claims 6 and 9 herein to independent form, incorporating the recitations of the base claim, independent Claim 1. Support for the claim amendments is apparent from the original claims. No new matter is added. Entry of the amendments pursuant to 37 C.F.R. §1.116 is proper, since the amendments merely adopt the Examiner's requirements as to form.

Response to issues presented under 35 U.S.C. §103

Claims 1-5, 7, 8, 10 and 11 stand rejected under 35 U.S.C. §103(a) as being unpatentable over international application number PCT/US97/22251 (publication number WO 98/24807). Specifically, the Examiner contends the reference teaches compounds of the formula set forth in Claim 1 wherein residue A⁶ can be Abu, beta-Ala, Gaba, or Val.

As previously pointed out by the Applicants and taught in the specification on page 2, lines 14-16, the peptides of the present invention are a previously undefined sub-genus encompassed by the genus of compounds disclosed and claimed in WO 98/24807. Similar to the compounds of the WO 98/24807 application, the compounds of the present invention, i.e., compounds of formula (I) (Claim 1), possess high affinity for somatostatin receptors. In contradistinction to the compounds of the WO 98/24807 application, however, the compounds of the present invention were surprisingly discovered to possess agonist activity. In the last response, Applicants submitted data via a Rule 132 affidavit supporting this distinction.

However, the Examiner has maintained the rejection, reasoning:

Applicants have stated in their specification that their claimed compounds have unexpected agonist as opposed to antagonist

activities...However, in the absence of a probative comparison of the closest prior art compounds of the WO Patent Application '807 and of Applicants' claimed compounds in the same assay, Applicants' statement in and of itself can not be relied upon to rebut the *prima facie* case of obviousness set forth above. (Office Action, page 3.)

Applicants submit that the Examiner has not made a *prima facie* case of obviousness. MPEP §2143.03 states that "[t]o establish *prima facie* obviousness of a claimed invention, all claim limitations must be taught or suggested by the prior art." (emphasis added.)

In rejecting the claims as obvious over the prior genus shown to possess Somatostatin antagonist activity, the Examiner is illogically concluding that it would have been obvious to one of ordinary skill in the art to make certain amino acid (including synthetic) substitutions and that the resulting compounds would possess Somatostatin *agonist* activity, not antagonist activity as taught and suggested by the prior art. However, this conclusion is neither taught nor suggested in the prior art of record. In fact, WO 98/24807 actually *teaches away from* the present invention, suggesting that the resulting compounds would possess antagonist activity. Applicants point out that obviousness cannot be established using Applicants' own disclosure as a guide for selecting and reconstructing the claimed invention. The CAFC has stated:

[T]he test of whether it would have been obvious...must still be met by *identification of some suggestion, teaching, or motivation in the prior art, arising from what the prior art would have taught a person of ordinary skill in the field of the invention. In re Dance*, 160 F.3d 1339, 1348, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998) (emphasis added).

Omitting a particular statement of the suggestion or motivation to combine prior art references to make a claimed invention simply amounts to hindsight reconstruction based on an inventor's own teachings. As the Court of Appeals for the Federal Circuit noted in *In re Dembiczak*:

Combining prior art references without evidence of such a suggestion, teaching, or motivation simply takes the inventor's disclosure as a blueprint for piecing together the prior art to defeat patentability -- the essence of hindsight. *In re Dembiczak*, 175 F.3d 994, 999; 50 USPQ2d 1614, 1617; 1999 WL 246572 (Fed.Cir. 1999).

In the present case, the Examiner is presuming a motivation in one of ordinary skill to select agonist compounds -- given only a teaching relating to antagonist compounds and without citing any teaching or suggestion from the prior art.

Accordingly, absent a teaching or suggestion in the art, Applicants submit that the Examiner has failed to make a *prima facie* case of obviousness and has improperly applied hindsight reasoning in rejecting the present claims as obvious over the genus.

The Examiner also contends that absent data comparing the antagonist compounds to the presently claimed agonist compounds, the peptide modifications of the present application are obvious over the previously disclosed genus of antagonist peptides, stating:

However, in the absence of a probative comparison of the closest prior art, i.e., compounds of the WO Patent Application '807 and of Applicants' claimed compounds in the same assay, Applicants' statement in and of itself can not be relied upon to rebut the *prima facie* case of obviousness set forth above. (Office Action, page 3.)

As discussed above, Applicants submit that the Examiner has not made a *prima facie* case of obviousness. Moreover, the comparison called for by the Examiner is only appropriate when the claimed compounds are suggested by prior art compounds expected to have the same properties, which is not the case here. *See, In re Jones*, 958 F.2d 347, 21 U.S.P.Q. 2d 1941 (Fed. Cir. 1992). In *Jones*, the applicants appealed to the Federal Circuit to set aside the BPAI decision affirming an obviousness rejection of a species not disclosed in, but admittedly encompassed by, a previously patented genus. The BPAI upheld the rejection of the particular salt as *prima facie* obvious in view of the genus reasoning that the claimed species was so "closely related in structure" to the genus, that "compounds similar in structure will have similar properties", and that the applicants' data and Rule 132 declarations failed to "compare the claimed subject matter with the closest prior art." 958 F.2d at 349.

The CAFC reversed the BPAI decision stating:

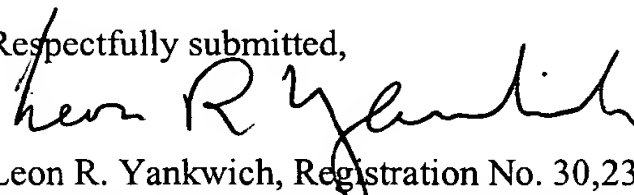
Conspicuously missing from this record is any *evidence*, other than the PTO's speculation (if it be called evidence) that one of ordinary skill in the herbicidal art would have been motivated to make the modifications of the prior art salts necessary to arrive at the claimed 2-(2'-aminoethoxy)ethanol salt. *See In re Grabiak*, 769 F.2d 729, 731, 226 U.S.P.Q. 870, 872 (Fed. Cir. 1985) ("In the case before us there must be adequate support in the prior art for the [prior art] ester/[claimed] thioester change in structure, in order to complete the PTO's *prima facie* case and shift the burden of going forward to the applicant."); *In re Lahu*, 747 F.2d 703, 705, 223 U.S.P.Q. 1257, 1258 (Fed. Cir. 1984) ("The prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound.") *Jones*, 958 F.2d at 351.

Similar to the situation in *Jones*, Applicants submit that the present case also lacks motivation or suggestion for one skilled in the art to search for agonist compounds within a genus of antagonists, that is, to make the substitutions leading to the compounds of the claims, guided only by the teachings of WO 98/24807. Moreover, there is certainly no suggestion in WO 98/24807 that making the correct selections would result in compounds discovered by Applicants to possess Somatostatin agonist activity. Absent such a teaching, the Examiner is grafting the motivation from Applicants' teachings onto the reference to inappropriately switch the burden of going forward to the Applicants.

Applicants have discovered a subgenus of agonist compounds within a field of agonists and have defined it with particularity. The WO 98/24807 reference does not lead a person of ordinary skill in the art to make the selections necessary to achieve compounds of the genus or to search among antagonists for agonists. The subgenus as defined in the claims is distinguished from the genus of the reference, and without a teaching in the art suggesting the invention comparative data is unnecessary: the capacity of the person of ordinary skill in the art has already been surpassed, further proof of the inventiveness of the claimed subgenus is not required by law.

Accordingly, since the compounds of the present invention possess advantageous and unexpected properties that could not have been perceived or imagined by those skilled in the art from consideration of WO 98/24807, and in fact the Examiner is unable to point to any suggestion in the art to make the claimed compounds or to expect the novel results, Applicants request reconsideration and withdrawal of the rejection of Claims 1-5, 7, 8, 10 and 11 under 35 U.S.C. §103(a).

Respectfully submitted,



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